IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:	Toranto *et al.*		
Serial No.:	09/976,872	Group No.:	1641
Filed:	10/12/2001	Examiner:	D. A. Davis
Entitled:	**ANALYTE DETECTION**		

APPELLANT'S BRIEF

APPEAL NO.:

Mail Stop Appeal Brief—Patents
Commissioner for Patents and Trademarks
P.O. Box 1450
Alexandria, VA 22313-1450

CERTIFICATE OF MAILING UNDER 37 C.F.R. § 1.10

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Date: 7/12/2004 By: Susan M. McClintock
Susan M. McClintock

Sir:

07/15/2004 HALI11 00000036 09976872
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This Brief is in furtherance of the Notice of Appeal.

The fees required under § 1.17(h) and any required Petition for Extension of Time for filing this Brief and fees therefore are dealt with in the accompanying TRANSMITTAL OF APPEAL BRIEF.

This Brief is transmitted in triplicate. [37 C.F.R. § 1.192(a)].

This Brief contains these items under the following headings and in the order set forth below [37 C.F.R. § 1.192(c)]:

I. REAL PARTY IN INTEREST

The real party in interest is the assignee of record, N2itive1 Innovations.

II. RELATED APPEALS AND INTERFERENCES

There are no related appeals or interferences known to Appellant or to Appellant's legal representative.

III. STATUS OF CLAIMS

Claims 1-73 were filed in the original application. During prosecution of the application, Claims 16-17 and 28-73 were cancelled. Claims 1-15 and 18-27 have been rejected by the Examiner in the latest and Final Office Action dated November 28, 2003. Therefore, Claims 1-15 and 28-73 are pending in this appeal. No other claims are pending. Appellant appeals the Final Office Action of November 28, 2003.

The Claims, as they now stand, are set forth in Appendix A.

IV. STATUS OF THE AMENDMENTS

With respect to the amendments of the Claims, Appellant's Amendment and Response of September 3, 2003 has been entered.

V. SUMMARY OF THE INVENTION

The present invention relates to analyte detection test systems, including test systems for the detection of analytes in oral fluids such as saliva. Analyte detection systems are known in the art. However, the tests available in the prior art suffer from various drawbacks. For

example, many of the tests are too expensive, cumbersome, complex, or dangerous for routine or frequent usage, rely on electronic equipment that is too complex or expensive for use by individuals outside of a laboratory or clinical setting, or utilize toxic materials preventing direct oral use. In addition, many individuals have an aversion to certain types of sample testing procedures, such as blood and urine testing, and would not be willing to self-administer such tests.

The present invention avoids the various drawbacks associated with traditional methods of analyte detection by providing compositions and methods for the detection of analytes using, for example, a safe, non-toxic, non-irritating, non-carcinogenic, inexpensive, durable, compact, accurate, painless, and easy to use oral testing system. The methods of the present invention improve both the safety and the utility of analyte detection, and represent a significant advance in the art.

VI. ISSUES

There are four issues involved in the present appeal:

Issue 1 – Whether the Examiner failed to properly consider the evidence submitted with Appellant's Amendment and Response of September 3, 2003.

Issue 2 – Whether Claims 1-4 and 11 are anticipated under 35 U.S.C. § 102(b) by Manautou *et al.* (U.S. Patent No. 3,875,013).

Issue 3 – Whether Claims 5-6, 8-15, and 18-27 are patentable under 35 U.S.C. § 103(a) over Manautou *et al.* in view of Bogema (U.S. Patent No. 6,248,598).

Issue 4 – Whether Claim 7 is patentable under 35 U.S.C. § 103(a) over Manautou *et al.* in view of Kindler (U.S. Patent No. 5,494,831).

VII. GROUPING OF CLAIMS

Each Claim stands alone. Each Claim has separate limitations and must be considered independently.

Independent Claim 1 specifies a method for detecting the presence of an analyte in saliva, comprising providing an assay test comprising a reaction site that produces a detectable signal in presence of an analyte, wherein said reaction site comprises a non-toxic chromogen; placing said reaction site into a mouth of a subject under conditions such that saliva from said subject is contacted with said reaction site; and detecting the presence or absence of said detectable signal in said reaction site.

Dependent Claim 2 specifies the method of Claim 1, wherein said detectable signal comprises a color change. Thus, prior art must further teach a color change.

Dependent Claim 3 specifies the method of Claim 1, wherein said assay test comprises a test strip. Thus, prior art must further teach a test strip.

Dependent Claim 4 specifies the method of Claim 3, wherein said test strip comprises an absorbent material, wherein said reaction site is located within said absorbent material. Thus, prior art must further teach an absorbent material, wherein said reaction site is located within said absorbent material.

Dependent Claim 5 specifies the method of Claim 1, wherein said reaction site comprises an enzyme, wherein said analyte is a substrate for said enzyme. Thus, prior art must further teach an enzyme, wherein said analyte is a substrate for said enzyme.

Dependent Claim 6 specifies the method of Claim 1, wherein said reaction site comprises an antibody, wherein said antibody binds to said analyte. Thus, prior art must further teach a reaction site that comprises an antibody, wherein said antibody binds to said analyte.

Dependent Claim 7 specifies the method of Claim 1, wherein said reaction site comprises a biosensor. Thus, prior art must further teach a reaction site that comprises a biosensor.

Dependent Claim 8 specifies the method of Claim 5, wherein said enzyme produces oxidation and reduction products when reacted with said analyte. Thus, prior art must further teach an enzyme wherein said enzyme produces oxidation and reduction products when reacted with said analyte.

Dependent Claim 9 specifies the method of Claim 8, wherein said reaction site further comprises a chromogen. Thus, prior art must further teach a reaction site that further comprises a chromogen.

Dependent Claim 10 specifies the method of Claim 8, wherein said chromogen undergoes a color change in the presence of said oxidation and reduction products. Thus, prior art must further teach a chromogen that undergoes a color change in the presence of said oxidation and reduction products.

Dependent Claim 11 specifies the method of Claim 2, wherein said color change is detectable by the human eye. Thus, prior art must further teach a color change that is detectable by the human eye.

Dependent Claim 12 specifies the method of Claim 1, wherein said reaction site is held in said mouth for a sufficient amount of time to generate said detectable signal while said reaction site is in said mouth. Thus, prior art must further teach a reaction site that is held in said mouth for a sufficient amount of time to generate said detectable signal while said reaction site is in said mouth.

Dependent Claim 13 specifies the method of Claim 1, wherein said reaction site is held in said mouth for a sufficient amount of time to generate a detectable signal faster than when said

reaction site is held in said mouth for 5 seconds. Thus, prior art must further teach a reaction site that is held in said mouth for a sufficient amount of time to generate a detectable signal faster than when said reaction site is held in said mouth for 5 seconds.

Dependent Claim 14 specifies the method of Claim 1, wherein said reaction site is held in said mouth for 10 seconds or more. Thus, prior art must further teach a reaction site that is held in said mouth for 10 seconds or more.

Dependent Claim 15 specifies the method of Claim 14, wherein said reaction site is held in said mouth for 30 seconds or more. Thus, prior art must further teach a reaction site that is held in said mouth for 30 seconds or more.

Dependent Claim 18 specifies the method of Claim 1, wherein said chromogen is a non-irritant. Thus, prior art must further teach a chromogen that is a non-irritant.

Dependent Claim 19 specifies the method of Claim 1, wherein said chromogen is not a known carcinogen. Thus, prior art must further teach a chromogen that is not a known carcinogen.

Dependent Claim 20 specifies the method of Claim 1, wherein said analyte comprises an alcohol moiety. Thus, prior art must further teach an analyte that comprises an alcohol moiety.

Dependent Claim 21 specifies the method of Claim 20, wherein said analyte comprises ethanol. Thus, prior art must further teach an analyte that comprises ethanol.

Dependent Claim 22 specifies the method of Claim 20, wherein said analyte comprises glucose. Thus, prior art must further teach an analyte that comprises glucose.

Dependent Claim 23 specifies the method of Claim 1, wherein said analyte comprises a ketone moiety. Thus, prior art must further teach an analyte that comprises a ketone moiety.

Dependent Claim 24 specifies the method of Claim 23, wherein said analyte comprises a ketone body. Thus, prior art must further teach an analyte that comprises a ketone body.

Dependent Claim 25 specifies the method of Claim 1, wherein said analyte comprises a prostate-specific antigen. Thus, prior art must further teach an analyte that comprises a prostate-specific antigen.

Dependent Claim 26 specifies the method of Claim 1, wherein said analyte comprises melatonin. Thus, prior art must further teach an analyte that comprises melatonin.

Dependent Claim 27 specifies the method of Claim 1, wherein said analyte comprises lactoferrin. Thus, prior art must further teach an analyte that comprises lactoferrin.

Because each of the Claims has different limitations, they do not stand or fall together. Rather, they must be evaluated separately.

VIII. ARGUMENT

A. Issue 1 - The Examiner Failed to Properly Consider the Appellant's Amendment and Response of September 3, 2003

The resolution of the four issues involved in the present appeal essentially hinges upon a single question: does the prior art cited by the Examiner provide a teaching of the use of a non-toxic chromogen for saliva-based analyte detection? For the reasons detailed below, the Appellant respectfully submits that the answer is no, as the Examiner has not provided, and cannot provide, evidence that refutes or even properly addresses the evidence proffered by the Appellant in its Amendment and Response of September 3, 2003.

1. The Final Office Action of November 28, 2003 is Procedurally Erroneous

Every claim of the present invention recites the novel element of a non-toxic chromogen. The Examiner argues that the Manautou *et al.* reference, alone and in combination with Bogema and Kindler, both anticipates and renders obvious the present invention by teaching the use of a non-toxic chromogen for saliva-based analyte detection. However, by the Examiner's own admission, this contention rests solely upon the unsubstantiated *assumption* that any chromogen taught for use in an orally administered test must be non-toxic. For example, the Examiner makes the following assertions:

> The reference of Manautou et al utilizes an oral test strip to test for pregnancy and the chromogen, p-nitrophenol is *apparently* in small enough amounts to be *assumed* safe and non-toxic... It would be *assumed* the [sic] instant reference of Manautou et al would encompass these known safety features, especially when patient [sic] is undergoing oral testing for detection of an analyte wherein said oral test strip utilizes a chromogen, one [sic] skilled in the art would *assume* that a chromogen that is non-irritating and non-toxic [sic].

November 28, 2003 Final Office Action at 6 *(emphasis added).*

This is akin to asserting that any product sold for human use at any time in history (the Appellant notes that Manautou *et al.* is over thirty years old) can safely be assumed to be non-hazardous, based on the assumption that no merchant would ever offer unsafe products for sale to the public, or even more tenuously, prophetically describe the use of an unsafe product in a patent. As the entire field of product liability law and the continuous removal of dangerous products from the marketplace illustrate, such assumptions are neither credible nor legally supportable.

In addition to being deeply flawed, the assumptions relied upon by the Examiner are wholly unsupported. Indeed, the Examiner has failed to provide any factual *evidence* whatsoever to support either the logic or the validity of her assumptions. More importantly, the Examiner

has failed to provide any factual evidence that refutes or even properly addresses the evidence provided by the Appellant in its Amendment and Response of September 3, 2003. The sole chromogen taught by Manautou *et al.* for use in orally administered tests is p-nitrophenol, a substance known to be highly toxic. The Appellant has submitted ample factual evidence of p-nitrophenol's high toxicity, and as the Examiner has presented no factual evidence to the contrary, the Appellant's evidence stands unrebutted. The rule mandating proper consideration of evidence in response to a 35 U.S.C. § 103 obviousness rejection was clearly articulated by the Federal Circuit in *In re Oetiker:* "After evidence or argument is submitted by the applicant in response, patentability is determined on the totality of the record, by a preponderance of evidence with due consideration to persuasiveness of argument." *In re Oetiker,* 977 F.2d 1443, 1445 (Fed. Cir. 1992); *see also* Manual of Patent Examining Procedure (M.P.E.P) § 2142. Because the record in this matter contains no factual evidence that p-nitrophenol is non-toxic, and ample, unrebutted factual evidence of its high toxicity, the preponderance of the evidence clearly favors the Appellant's position. Moreover, since the Examiner, while failing to provide factual evidence to the contrary, nonetheless chose to disregard the factual evidence provided by the Appellant, it is clear that the Examiner failed to give due consideration to the persuasiveness of the Appellant's arguments. Because the Examiner has provided no factual evidence, but instead has based her entire argument on improper assumptions and speculative conclusions, the Appellant has been denied a procedural consideration to which it is legally entitled. For these reasons, the Final Office Action of November 28, 2003 was procedurally erroneous, and warrants reversal.

2. The Final Office Action of November 28, 2003 is Factually Erroneous

Even if the Examiner had properly considered the evidence and arguments presented by the Appellant, the argument upon which the claim rejections are based is factually erroneous (which perhaps explains why no evidence was cited by the Examiner). The sole chromogen taught by Manautou *et al.,* upon which all of the rejections are principally based, is p-nitrophenol, a compound known for its toxicity. In support of this, Appellant submits herewith as Appendix B a data sheet from NTP Chemical Repository describing the toxic properties of p-nitrophenol. In particular, Appellant notes the following characteristics related to ingestion of, or skin contact with, p-nitrophenol: "This compound is highly toxic by ingestion, inhalation or absorption through the skin. When heated to decomposition it emits toxic fumes. It is corrosive to the skin . . . Phenols are very toxic poisons AND corrosive and irritating, so that inducing vomiting may make medical problems worse." NTP Chemical Repository Data Sheet printout, pages 3-5. Although this evidence was submitted by the Appellant in its Amendment and Response of September 3, 2003, the Examiner has provided no factual evidence to the contrary. Rather, the Examiner has simply speculated that the p-nitrophenol taught by Manautou *et al.* is "*apparently* in small enough amounts to be assumed safe and non-toxic." November 28, 2003 Final Office Action at 6 *(emphasis added).* In addition to the fact that the Examiner provides no factual evidence, there is also no factual basis for her assertion that the amount taught may be "assumed safe and non-toxic," since the Manautou *et al.* reference does not even specify the amount of p-nitrophenol to use. The Appellant respectfully submits, however, that p-nitrophenol is highly toxic even at very low levels, as indicated by an array of evidence provided previously and available from numerous public sources. For example, according to the U.S. Department of Health and Human Services, the oral *lethal* dose of p-nitrophenol in adult rats is approximately

five thousands of an ounce. U.S. Department of Health and Human Services, Registry of Toxic Effects of Chemical Substances, National Toxicology Information Program, National Library of Medicine, 1993 (data also provided in the NTP Chemical Repository Data Sheet cited above).

As explained above, the Examiner has similarly failed to provide any factual evidence whatsoever to support her contention that an invention designed for oral use can be assumed to be safe. However, as the entire history of modern medicine illustrates, the mere fact that a product for oral use is disclosed in a reference is no guarantee that the product is safe or useful. For example, thalidomide, which can cause severe birth defects, was widely prescribed by doctors in the 1950s to treat nausea and insomnia in pregnant women. The fact that thalidomide was prescribed for pregnant women clearly would not support a conclusion that it was safe. Thus, just as the Examiner could not cite a fifty year old thalidomide reference to reject a claim to a non-mutagenic compound based on prior use of the compound, she likewise cannot cite a thirty year old p-nitrophenol reference to reject a claim to a non-toxic chromogen, where the reference simply suggests use—but does not provide toxicity data or in any way indicate that the p-nitrophenol in the device is non-toxic.

B. Issue 2 – The Claims Are Not Anticipated by Manautou *et al.*

The Examiner has rejected Claims 1-4 and 11 under 35 U.S.C. § 102(b) as allegedly being anticipated by Manautou *et al.* November 28, 2003 Final Office Action at 2. The Federal Circuit has stated the relevant analysis for anticipation as follows: "A claim is anticipated only if each and every element as set forth in the claims is found, either expressly or inherently described, in a single prior art reference." *Verdegaal Bros. v. Union Oil of California,* 2

U.S.P.Q.2d 1051, 1053 (Fed. Cir. 1987). Appellant respectfully submits that the reference cited by the Examiner does not teach each element of the Claims.

Specifically, as explained above, the Manautou *et al.* reference contains no teaching of the use of a non-toxic chromogen, which is a novel and essential element of the presently claimed invention. Rather, Manautou *et al.* teaches the use of p-nitrophenol, a compound known for its high toxicity. The Examiner has not cited, and cannot cite, evidence that p-nitrophenol-based test strips have been found safe for oral use, or have found such use in the real-world marketplace. The Appellant has cited substantial evidence, on the other hand, of p-nitrophenol's high toxicity, and consequent unsuitability for oral use of the type contemplated by the presently claimed invention. Moreover, the non-toxic chemistry of the present invention is in widespread public use, and has met with great commercial success. Because Manautou *et al.* fails to teach the use of a non-toxic chromogen, it consequently fails to teach each element of the claims of the present invention. Accordingly, the Appellant respectfully submits that Claims 1-4 and 11 are not anticipated by Manautou *et al.*, and requests that the rejection be reversed..

C. Issue 3 – Whether the Claims are patentable under 35 U.S.C. § 103(a) over Manautou *et al.* in view of Bogema (U.S. Patent No. 6,248,598)

The Examiner has rejected Claims 5-6, 8-15, and 18-27 as allegedly being unpatentable over Manautou *et al.* in view of Bogema. November 28, 2003 Final Office Action at 3. Appellant respectfully submits, however, that the Examiner has failed to establish a *prima facie* case of obviousness. Under M.P.E.P. § 2143, there are three basic criteria that must be met to provide a *prima facie* showing of obviousness. The first is that "there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings." The

second is that "there must be a reasonable expectation of success" should the combination be carried out. The third is that "the prior art reference (or references when combined) must teach or suggest all the claim limitations." Since all three criteria are must be present, failure to establish even one of these requirements means that the Examiner has failed to establish a *prima facie* case of obviousness. In this case, the Examiner has failed to establish all of the three criteria necessary to support a rejection under 35 U.S.C. § 103(a).

As explained above, Manautou *et al.* contains no teaching of a non-toxic chromogen for oral testing. Indeed, none of the prior art cited by the Examiner, including the Bogema reference, teaches the use of a non-toxic chromogen for oral testing. Thus, there is no teaching of all of the claim limitations of the presently claimed invention in the cited art, alone or in combination. As such, there can also be no reasonable expectation of success in combining the cited references to achieve the presently claimed invention, since an essential element is absent. Moreover, the wholesale lack of a teaching of the use of a non-toxic chromogen for oral testing in the prior art is further evidence of the nonobvious nature of the presently claimed invention. The Appellant respectfully submits that, because there is no teaching of the use of a non-toxic chromogen, the Examiner has failed to set forth a *prima facie* showing of obviousness under M.P.E.P. § 2143. The Appellant thus respectfully requests that the rejection be reversed.

D. Issue 4 – Whether the Claims are patentable under 35 U.S.C. § 103(a) over Manautou *et al.* in view of Kindler (U.S. Patent No. 5,494,831)

The Examiner has rejected Claim 7 under 35 U.S.C. § 103(a) as allegedly being unpatentable over Manautou *et al.* in view of Kindler. November 28, 2003 Final Office Action at 5. The Appellant respectfully disagrees, and submits that the Examiner has failed to set forth a *prima facie* showing of obviousness as required under M.P.E.P. § 2143.

As discussed above, none of the prior art cited by the Examiner, including both the Manautou *et al.* and Kindler references, teaches the use of a non-toxic chromogen for oral testing. Thus, there is no teaching of all of the claim limitations of the presently claimed invention in the cited art, alone or in combination. As such, there can also be no reasonable expectation of success in combining the cited references to achieve the presently claimed invention, since an essential element is absent. As stated above, the absence of a teaching of the use of a non-toxic chromogen for oral testing in the prior art is further evidence of the nonobvious nature of the presently claimed invention. The Appellant respectfully submits that, because there is no teaching of the use of a non-toxic chromogen, the Examiner has failed to set forth a *prima facie* showing of obviousness under M.P.E.P. § 2143. The Appellant thus respectfully requests that the rejection be reversed.

E. Conclusion

For the foregoing reasons, it is submitted that the Examiner's rejection of Claims 1-15 and 18-27 was erroneous, and reversal of the rejection is respectfully requested. The Appellant requests either that the Board render a decision as to the allowability of the claims, or alternatively, that the application be remanded for reconsideration by the Examiner.

Dated: 7/12/04 By: _____

David A. Casimir
Registration No. 42,395

MEDLEN & CARROLL, LLP
101 Howard Street, Suite 350
San Francisco, California 94105

APPENDIX A

PENDING CLAIMS

The following is a list of the pending Claims.

1. (previously presented) A method for detecting the presence of an analyte in saliva, comprising:

   a) providing an assay test comprising a reaction site that produces a detectable signal in presence of an analyte; wherein said reaction site comprises a non-toxic chromogen;

   b) placing said reaction site into a mouth of a subject under conditions such that saliva from said subject is contacted with said reaction site; and

   c) detecting the presence or absence of said detectable signal in said reaction site.

2. (original) The method of Claim 1, wherein said detectable signal comprises a color change.

3. (original) The method of Claim 1, said assay test comprises a test strip.

4. (original) The method of Claim 3, wherein said test strip comprises an absorbent material, wherein said reaction site is located within said absorbent material.

5. (original) The method of Claim 1, wherein said reaction site comprises an enzyme, wherein said analyte is a substrate for said enzyme.

6. (original) The method of Claim 1, wherein said reaction site comprises an antibody, wherein said antibody binds to said analyte.

7. (original) The method of Claim 1, wherein said reaction site comprises a biosensor.

8. (original) The method of Claim 5, wherein said enzyme produces oxidation and reduction products when reacted with said analyte.

9. (original) The method of Claim 8, wherein said reaction site further comprises a chromogen.

10. (original) The method of Claim 8, wherein said chromogen undergoes a color change in the presence of said oxidation and reduction products.

11. (original) The method of Claim 2, wherein said color change is detectable by the human eye.

12. (original) The method of Claim 1, wherein in step b), said reaction site is held in said mouth for a sufficient amount of time to generate said detectable signal while said reaction site is in said mouth.

13. (original) The method of Claim 1, wherein in step b), said reaction site is held in said mouth for a sufficient amount of time to generate a detectable signal faster than when said reaction site is held in said mouth for 5 seconds.

14. (original) The method of Claim 1, wherein in step b), said reaction site is held in said mouth for 10 seconds or more.

15. (original) The method of Claim 14, wherein in step b), said reaction site is held in said mouth for 30 seconds or more.

18. (previously presented) The method of Claim 1, wherein said chromogen is a non-irritant.

19. (previously presented) The method of Claim 1, wherein said chromogen is not a known carcinogen.

20. (original) The method of Claim 1, wherein said analyte comprises an alcohol moiety.

21. (original) The method of Claim 20, wherein said analyte comprises ethanol.

22. (original) The method of Claim 20, wherein said analyte comprises glucose.

23. (original) The method of Claim 1, wherein said analyte comprises a ketone moiety.

24. (original) The method of Claim 23, wherein said analyte comprises a ketone body.

25. (original) The method of Claim 1, wherein said analyte comprises prostate-specific antigen.

26. (original) The method of Claim 1, wherein said analyte comprises melatonin.

27. (original) The method of Claim 1, wherein said analyte comprises lactoferrin.

APPENDIX B

NTP CHEMICAL REPOSITORY DATA SHEET FOR P-NITROPHENOL

NTP CHEMICAL REPOSITORY
P-NITROPHENOL

-IDENTIFIERS
 ===========

*CATALOG ID NUMBER: 000049

*CAS NUMBER: 100-02-7

*BASE CHEMICAL NAME: NITROPHENOL,P-

*PRIMARY NAME: P-NITROPHENOL

*CHEMICAL FORMULA: C6H5NO3

*STRUCTURAL FORMULA: OHC6H5NO2

*WLN: WNR DQ

*SYNONYMS:
  4-HYDROXYNITROBENZENE
  P-NITRO-PHENOL
  4-NITROPHENOL
  NCI-C55992
  PNP
  PARA-NITROPHENOL
  PHENOL, P-NITRO-
  UN 1663
  PHENOL, 4-NITRO
  NIPHEN
  P-HYDROXYNITROBENZENE
  MONONITROPHENOL

-PHYSICAL CHEMICAL DATA
 ======================

*PHYSICAL DESCRIPTIONS: LITERATURE: Colorless to slightly yellow crystals
                        REPOSITORY: Beige solid

*MOLECULAR WEIGHT: 139.11

*SPECIFIC GRAVITY: 1.270 @ 20/4 C

*DENSITY: 1.479-1.495 g/mL @ 20 C

*MP (DEG C): 113-115 C (Sublimes)

*BP (DEG C): 279 C (Decomposes)

*SOLUBILITIES:
       WATER : <0.1 mg/mL @ 21 C (RAD)

        DMSO : >=100 mg/mL @ 21 C (RAD)

 95% ETHANOL : >=100 mg/mL @ 21 C (RAD)

    METHANOL : Not available

     ACETONE : >=100 mg/mL @ 21 C (RAD)

     TOLUENE : Soluble

OTHER SOLVENTS:
Carbon disulfide: Slightly soluble
Pyrimidine: Soluble
Chloroform: Very soluble
Fixed alkali hydroxides: Soluble
Carbonates: Soluble
Ether: Very soluble
Benzene: Soluble in hot; slightly soluble in cold

*VOLATILITY:
Vapor pressure: 1 mm Hg @ 20 C; 18.7 mm Hg @ 186 C; 2.2 mm Hg @ 146 C
Vapor density : 1.244 @ 65 C

*FLAMMABILITY(FLASH POINT):
The flash point for this chemical is 192 C (377 F). It is combustible. Fires involving this compound should be controlled using a dry chemical, carbon dioxide or Halon extinguisher.

*UEL: Not available LEL: Not available

*REACTIVITY:
This compound is incompatible with oxidizing agents, organics, combustible substances and reducing agents.

*STABILITY:
This compound is stable under normal laboratory conditions. Solutions of this chemical in water, DMSO, 95% ethanol or acetone should be stable for 24 hours under normal lab conditions (RAD).

*OTHER PHYSICAL DATA:
Odorless
Sweet then burning taste
Freezing point: 113 C
Slightly volatile with steam

-TOXICITY
========

*NIOSH REGISTRY NUMBER: SM2275000

*TOXICITY: **(abbreviations)**

typ. dose	mode	specie	amount	unit	other
LD50	orl	rat	250	mg/kg	
LDLo	scu	rat	200	mg/kg	
LD50	orl	mus	380	mg/kg	
LD50	ipr	mus	75	mg/kg	
LDLo	ivn	dog	10	mg/kg	
LD50	unr	cat	150	mg/kg	
LDLo	scu	gpg	200	mg/kg	
LDLo	ims	pgn	65	mg/kg	
LDLo	scu	frg	60	mg/kg	
LD50	orl	mam	247	mg/kg	
LD50	skn	mam	920	mg/kg	

*AQTX/TLM96: Not available

*SAX TOXICITY EVALUATION:
THR = HIGH via oral, subcutaneous, intraperitoneal, intravenous and intramuscular routes.

*CARCINOGENICITY:
Status: NTP Carcinogenesis Studies; on test, November 1985

*MUTATION DATA:

test	lowest dose	test	lowest dose
dnd-esc	50 umol/L	dnr-omi	10 mg/plate
mrc-smc	21 mmol/L	dni-hmn:fbr	1 mmol/L

*TERATOGENICITY (Reproductive Effects Data): Not available

*STANDARDS, REGULATIONS & RECOMMENDATIONS:
OSHA: None
ACGIH: None
NIOSH Criteria Document: None
NFPA Hazard Rating: Health (H): None
Flammability (F): None
Reactivity (R): None

*OTHER TOXICITY DATA:
Review: Toxicology Review
Standards and Regulations: DOT-IMO: Poison B; Label: St. Andrews Cross
Status: Reported in EPA TSCA Inventory, 1983
EPA Genetic Toxicology Program, January 1984
Meets criteria for proposed OSHA Medical Records Rule

-OTHER DATA (Regulatory)
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*PROPER SHIPPING NAME (IATA): Nitrophenols

*UN/ID NUMBER: UN1663

*HAZARD CLASS: 6.1 SUBSIDIARY RISK: None PACKING GROUP: III

*LABELS REQUIRED: Keep away from food

*PACKAGING: PASSENGER: PKG. INSTR.: 619, Y619 MAXIMUM QUANTITY: 100 kg, 10 kg
CARGO : PKG. INSTR.: 619 MAXIMUM QUANTITY: 200 kg

*SPECIAL PROVISIONS: None

*USES:
Indicator in 0.1% alcohol solution, intermediate in organic synthesis, production of parathion, fungicide for leather, indicator in water analysis, bactericide.

*COMMENTS:
Reviewed by: RLT/860626

-HANDLING PROCEDURES
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*ACUTE/CHRONIC HAZARDS:
This compound is highly toxic by ingestion, inhalation or absorption through the skin. When heated to decomposition it emits toxic fumes. It is corrosive to the skin.

*MINIMUM PROTECTIVE CLOTHING:
If Tyvek-type disposable protective clothing is not worn during handling of this chemical, wear disposable Tyvek-type sleeves taped to your gloves.

*RECOMMENDED GLOVE MATERIALS:
Recommended Glove Type For Use With Neat (Undiluted) Chemical:
Recommendations based on permeation test results are made for handling the neat (undiluted) chemical. If this chemical makes direct contact with

your glove, or if a tear, puncture or hole develops, replace them at once.

Suggested Glove Type(s) (RAD): No information available

*RECOMMENDED RESPIRATOR:
Where the neat test chemical is weighed and diluted, wear a NIOSH-approved half face respirator equipped with an organic vapor/acid gas cartridge (specific for organic vapors, HCl, acid gas and SO2) with a dust/mist filter.

*OTHER: Not available

*STORAGE PRECAUTIONS:
You should store this chemical under refrigerated temperatures, and keep it away from oxidizing materials. STORE AWAY FROM SOURCES OF IGNITION.

*SPILLS AND LEAKAGE:
Should a spill occur while you are handling this chemical, FIRST REMOVE ALL SOURCES OF IGNITION, then you should dampen the solid spill material with 60-70% ethanol and transfer the dampened material to a suitable container. Use absorbent paper dampened with 60-70% ethanol to pick up any remaining material. Seal the absorbent paper, and any of your clothes, which may be contaminated, in a vapor-tight plastic bag for eventual disposal. Solvent wash all contaminated surfaces with 60-70% ethanol followed by washing with a soap and water solution. Do not reenter the contaminated area until the Safety Officer (or other responsible person) has verified that the area has been properly cleaned.

*DISPOSAL AND WASTE TREATMENT:
You should dispose of all waste and contaminated materials associated with this chemical as specified by existing local, state and federal regulations concerning hazardous waste disposal. It is suggested that your contaminated materials should be destroyed by incineration in a special, high temperature (>2000 degrees F), chemical incinerator facility.

-EMERGENCY PROCEDURES

*SKIN CONTACT:
IMMEDIATELY flood affected skin with water while removing and isolating all contaminated clothing. Gently wash all affected skin areas thoroughly with soap and water.
IMMEDIATELY call a hospital or poison control center even if no symptoms (such as redness or irritation) develop.
IMMEDIATELY transport the victim to a hospital for treatment after washing the affected areas.

*INHALATION:
IMMEDIATELY leave the contaminated area; take deep breaths of fresh air. If symptoms (such as wheezing, coughing, shortness of breath, or burning in the mouth, throat, or chest) develop, call a physician and be prepared to transport the victim to a hospital.
Provide proper respiratory protection to rescuers entering an unknown atmosphere. Whenever possible, Self-Contained Breathing Apparatus (SCBA) should be used; if not available, use a level of protection greater than or equal to that advised under Respirator Recommendation.

*EYE CONTACT:
First check the victim for contact lenses and remove if present. Flush victim's eyes with water or normal saline solution for 20 to 30 minutes while simultaneously calling a hospital or poison control center.
Do not put any ointments, oils, or medication in the victim's eyes without specific instructions from a physician.

IMMEDIATELY transport the victim after flushing eyes to a hospital even if no symptoms (such as redness or irritation) develop.

*INGESTION:

DO NOT INDUCE VOMITING. Phenols are very toxic poisons AND corrosive and irritating, so that inducing vomiting may make medical problems worse. IMMEDIATELY call a hospital or poison control center and locate activated charcoal, egg whites, or milk in case the medical advisor recommends administering one of them.

If advice from a physician is not readily available and the victim is conscious and not convulsing, give the victim a glass of activated charcoal slurry in water or, if this is not available, a glass of milk, or beaten egg whites and IMMEDIATELY transport victim to a hospital.

If the victim is convulsing or unconscious, do not give anything by mouth, assure that the victim's airway is open and lay the victim on his/her side with the head lower than the body. DO NOT INDUCE VOMITING. IMMEDIATELY transport the victim to a hospital.

*SYMPTOMS:

Symptoms following exposure to this compound may include irritation of the skin, eyes, nose and throat, headache, loss of consciousness, drowsiness, nausea, cyanosis, liver and kidney damage, methemoglobinemia, central nervous system depression, dyspnea, sweating, dry throat, fever, muscular weakness, fatigue, irritability, abdominal cramps, dermatitis, corneal damage and hypothermia.

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